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REMARKS

Claims 1-30 are in the case. The claims have been made subject to a requirement to restrict. Invention 1 encompassing claims 1-18, and 29 and the species of metal nanoparticles was provisionally elected. Applicants hereby affirm this election. Claims 19-28 and 30 are withdrawn as drawn to a non-elected invention. The examiner has withdrawn Claims 8 and 9 as drawn to a non-elected invention. Applicants reserve the right to have claims 8 and 9 rejoined subject to the allowance of all other claims based on an examination of the elected species.

No new matter has been added.

Claim Rejections – 35 USC § 103

Claims 1-7, 10-18 and 29 are rejected under 35 USC § 103(a) as being unpatentable over Subramaniam et al (US 6113795) (hereinafter "Subramaniam") and Templeton et al (Langmur, 1999, 15, pp 66-76) (hereinafter "Templeton") in view of Panek et al (US 4143026) (hereinafter "Panek") and Colman et al (US 6384297) (hereinafter "Colman").

The examiner suggests that Subramaniam describes a process and apparatus for the separation of nanoparticles from organic solvents. This process utilizes a filter or separator to separate particles that are precipitated from an organic solvent by the addition of a supercritical antisolvent, such as supercritical carbon dioxide. The application of this process to the separation of stabilized, water-soluble nanoparticles as describe in the present invention is not taught.

Templeton is cited for the teaching of water-soluble gold nanoparticles, stabilized by monolayers of tiopronin or coenzyme A.

Panek is cited for the teaching that dissolved polymers can be coagulated and precipitated by adding liquids in which the polymer is not soluble.

Colman is cited for the teaching that salts may be used to precipitate polymers in solution.

It is the examiner's opinion that the skilled person would know how to combine the separation methods of '795 with the monolayer coated nanoparticles of Templeton in combination with the understandings of methods of polymer precipitation as taught in '026 and '297 to derive the present invention. Applicants respectfully traverse.

It is axiomatic that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP 2143

Applicants submit that the present rejection fails in that there is no suggestion or

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motivation to combine the cited references, because the combined references do not teach all of the claim limitations, and because that the skilled person combining the cited references would have no reasonable expectation of success.

The instant invention claims a method for obtaining a population of stabilized, charged, water-soluble nanoparticles having a narrow size distribution from a population of nanoparticles having a broad size distribution using a combination of electrolyte and addition of a substantially water-miscible organic solvent. The addition of the substantially water-miscible organic solvent may be optionally repeated one or more times to obtain other fractions of particles having different narrow size distributions. Thus, the method is a size selective precipitation, i.e., fractionation.

Size distribution fractionation is an essential limitation of the invention as claimed, however this limitation is not suggested or taught by the cited references, either separately or in combination, and there is no direction to the skilled person in any of the references suggesting that size distribution fractionation would be possible if the reference were combined.

The examiner suggests that Applicants have admitted that fractionating gold particles from organic solvents by the addition of a non-solvent were known (see page 4 of the action). The statement referred to by the examiner is made in reference to Whetten et al. (Adv. Mater. 8:428-433 (1996)), who describe a method for fractionating gold nanoparticles from organic solvents by incremental addition of a non-solvent. However, there is no teaching or suggestion in that disclosure that stabilized, charged, water-soluble nanoparticles may be fractionated (i.e., precipitated in a size selective manner) from an aqueous solution using a combination of electrolyte and the addition of a substantially water-miscible organic solvent, as is claimed in the instant invention.

The examiner suggests that Subramaniam teach fractionation of particles may be carried out by introducing a an anti-solvent to a solution of particles (col. 3, line 7-32). Applicants submit that Subramaniam does not teach fractionation of "particles" as they are described and defined in the present specification ("...metallic or semiconductor particles with an average particle diameter of between 1 and 100 nm." Page 6, line 3) but rather teach the separation of drug molecules and polymers (see example 3 of Subramaniam for example).

Subramaniam et al. describe a process and apparatus for continuously harvesting drugs or polymers from organic solution-laden near critical and supercritical fluids. The method described pertains to the recovery of drugs or polymers using an antisolvent which is a supercritical fluid. The disclosure does not teach or suggest that stabilized, charged, water-soluble nanoparticles (which are inorganic particles) would behave in the same way as drug molecules and polymers (which are organic molecules). Additionally, the antisolvents described are supercritical fluids (e.g. carbon dioxide, propane, butane, isobutane, nitrous oxide, sulfur hexafluoride, hydrogen, etc.), not water-miscible organic solvents as taught in

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the instant invention. Moreover, Subramaniam et al. do not teach or suggest that a size-selective precipitation of nanoparticles may be achieved by using a combination of electrolyte and water-miscible organic solvent.

The examiner suggests that Templton supplies the qualities of the nanoparticles not described by Subramaniam. Templeton et al. does describe water-soluble gold nanoparticles that are stabilized by monolayers of tiopronin or coenzyme A. They also describe that these nanoparticles are completely insoluble in methanol but are quite soluble in water. However, there is no teaching or suggestion in that disclosure that these stabilized, charged, water-soluble nanoparticles may be fractionated (i.e., precipitated in a size selective manner) using a combination of electrolyte and the addition of a substantially water-miscible organic solvent, as is claimed in the instant invention. The mere teaching of water soluble particle by Templton does not supply motivation to combine with Subramaniam who does not teach a method applicable to the particles of the present invention.

The examiner suggests that Panek teaches the utility of an electrolyte in the present method. Panek et al. teach that dissolved polymers or polymers suspended in water or in organic solvents may be deposited onto surfaces of inorganic solids by precipitation with inorganic salts or by adding suitable liquids in which the polymer is insoluble. However there is no teaching or suggestion that stabilized, charged, water-soluble nanoparticles (which are inorganic particles) would behave in the same way as organic polymers. Additionally, Panek et al. do not teach or suggest that a size-selective precipitation of nanoparticles may be achieved by using a combination of electrolyte and water-miscible organic solvent. Therefore, Panek et al. do not teach or suggest that stabilized, charged, water-soluble nanoparticles may be fractionated (i.e., precipitated in a size selective manner) using a combination of electrolyte and the addition of a substantially water-miscible organic solvent, as is claimed in the instant invention.

Finally Colman et al. teach that it is well known that addition of a neutral inorganic salt to an aqueous solution of a water-soluble polymer may force polymer precipitation through a salting out phenomenon. Again, this teaching deals with organic polymers, not stabilized, charged, water-soluble nanoparticles. Additionally, Colman et al. teach only precipitation, not size-selective precipitation (i.e., fractionation). Therefore, Colman et al. do not teach or suggest that stabilized, charged, water-soluble nanoparticles may be fractionated (i.e., precipitated in a size selective manner) using a combination of electrolyte and the addition of a substantially water-miscible organic solvent, as is claimed in the instant invention.

In summary, Subramaniam, Panek and Colman contain teaching relevant to precipitation of organic polymers. The examiner combines the teachings of these references with Templton teaching a water-soluble gold nanoparticle that is stabilized by monolayer, to suggest that the invention is obvious. Applicants submit that the skilled person would have no

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motivation to look to Subramanium, Panek and Colman for the fractionation of the particles of Templton as the processes in Subramanium, Panek and Colman are developed for a different materials. Additionally the key limitation of size distribution fractionation is completely missing from all of the cited references, in violation of the third prong of the test for a prima facia case under 35 USC § 103.

In view of the foregoing arguments applicants respectfully request the examiner reconsider the rejection under 35 USC § 103 and allow the claims in their present form.

Respectfully submitted,



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